Radiosensitization & Hyperthermia as Cancer Therapy

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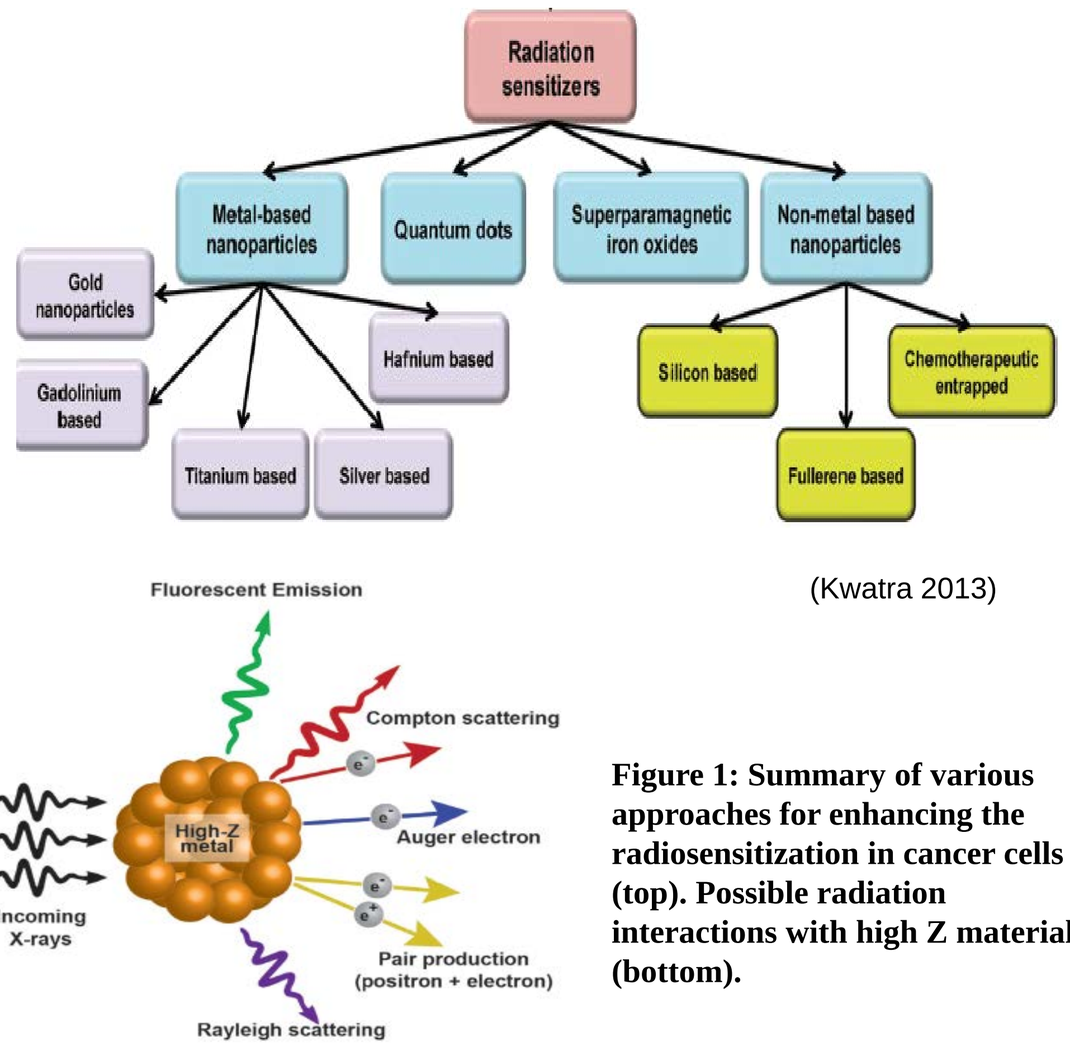
Background

Radiation therapy along with surgery and chemotherapy are the major therapeutic strategies for cancer treatment. It involves the delivery of high intensity ionizing radiation with high accuracy to the tumor tissue resulting in the death of tumor cells. Radiation sensitization is a process of enhancing the susceptibility of tumor tissues to injury by radiation exposure. Hence, radiosensitizers are therapeutic or otherwise inert agents that enhance the effects of radiation therapy.[1] Hyperthermia (also called thermal therapy or thermotherapy) is a type of cancer treatment in which body tissue is exposed to high temperatures (up to 45°C). Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy. Hyperthermia may make some cancer cells more sensitive to radiation or harm other cancer cells that radiation cannot damage. When hyperthermia and radiation therapy are combined, they are often given within an hour of each other. Hyperthermia can also enhance the effects of certain anticancer drugs. Magnetic nanoparticles (MNP) can induce localized hyperthermia when exposed to an alternating magnetic field (AMF).[3,4]



(Kwatra 2013)

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Figure 1: Summary of various approaches for enhancing the radiosensitization in cancer cells (top). Possible radiation interactions with high Z materials (bottom).

Quantum dots as Radiosensitizers: The mechanism of action for these is based on the principle of generation of radicals upon absorption of visible light by the quantum dots. Since these light waves have much less toxicity as compared X-rays or gamma rays, the overall adverse effects of the therapy are greatly reduced. The major disadvantage of this approach is that light waves within the visible spectrum have very little penetration depth and hence the therapies designed utilizing these mechanisms will be suitable only for superficial cancers.[1]

Gold Nanoparticles: Gold is biocompatible and it enhances the effect of the radiation over a large area of tumor thus eliminating the need of the nanoparticles to be delivered to all the cells of the tumor tissue. It is much easier to perform overall and tissue specific pharmacokinetic studies with the gold nanoparticles as they are easy to image and quantify. Thus the dose levels can be optimized for best results.[1]

$ZnFe_2O_4$ Nanoparticle: Zinc-iron oxide particles have an effective atomic number higher than the effective atomic number of the body's tissues. When used as a radiosensitizer, these nanoparticles showed increase in absorbed dose and increase in radiation effect of the therapy.[2]

Fe_3O_4 Nanoparticles: Magnetic nanoparticles are promising materials for hyperthermia treatment, as well as radiation sensitizing agents. Relative to other nanoparticles considered for radiation sensitization, they are highly biocompatible, and well suited for adjuvant hyperthermia applications.[6]

<u>Hypothesis: the addition of MNP to ionizing radiation increases the production of reactive oxygen species (ROS).</u>

By increasing the DNA damage due to ROS, MNP have the potential to potentiate local radiation. Whether ROS production is increased by the presence of MNP will be examined through *in vitro* studies which utilize the Dichloro-dihydro-fluorescein diacetate (DCFH-DA) assay to measure the changes in ROS due to the presence of MNP.[7] Related to this concept, is the question whether intracellular vs. extracellular MNP are more effective at generating cytotoxicity. Significant efforts have been made to increase the intracellular nature of MNP as a means of inducing intracellular heating with AMF exposure. Whether there are significant benefits or differences resulting from intracellular heating remain unresolved in the field. Furthermore, the difference in cytotoxicity of intracellular vs. extracellular MNP combined with radiation is also not understood. Variables will include not only intracellular vs. extracellular MNP, but cell density (pelleted vs. isolated plated cells), and radiation type and energy. Finally, the addition of AMF induced heating will also be included to determine its effect on both the achieved cytotoxicity and ROS levels.[5]

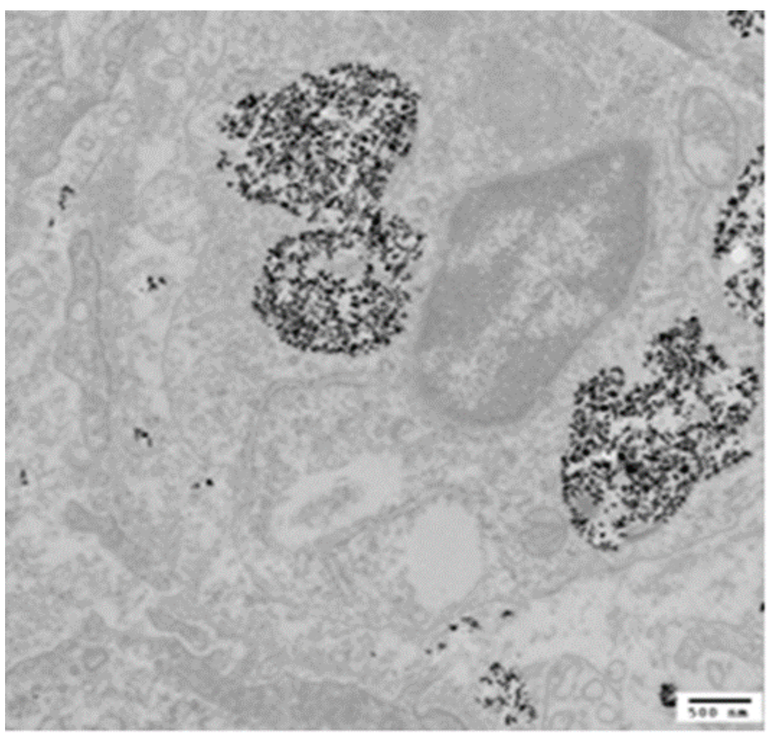

Figure 2: Transmission electron microscopy image of MNP located within an MTGB mouse mammary adenocarcinoma cell, following intratumoral injection. The clustering and intracellular uptake near nucleus may enhance the cytotoxicity of radiation therapy.

References

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